

Clostridium ramosum Bacteremia: Clinical Significance and Outcomes in a Multicenter Retrospective Cohort

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Abstract

Background:

Clostridium ramosum (*C. ramosum*) is an anaerobic gram-positive bacillus of the human intestine and a rare cause of bacteremia. This retrospective cohort study evaluated clinical characteristics and outcomes of a multicenter cohort of adults with *C. ramosum* bacteremia.

Methods:

This multicenter retrospective cohort included adults (≥ 18 years) with true *C. ramosum* bacteremia at Mayo Clinic hospitals in Arizona, Florida, Minnesota, and Wisconsin from September 1, 2012, through December 31, 2025. Data were collected through search for *C. ramosum* in microbiological culture records. Clinical characteristics assessed included immune status, source of bacteremia, presence of sepsis, neutropenic fever, monomicrobial vs. polymicrobial bacteremia, antimicrobial resistance patterns, antimicrobial therapy, length of stay and 30-day all cause mortality. Exploratory odds ratios (ORs) with 95% confidence intervals (CIs) were reported.

Results:

Among 90 patients with a positive *C. ramosum* blood culture, 17 were classified as contaminants and 73 comprised the study cohort. Median age was 66.0 years (IQR, 56.0–75.0); 44 (60.3%) were male and 33 (45.2%) were immunocompromised (including 26 with active malignancy, while the remaining 7 were received biologic immunosuppression). The most common infection sources were gastrointestinal (32/73, 43.8%) and central line-related (8/73, 11%). At presentation, 50.7% of patients met criteria for sepsis and 15/73 (20.5%), were in septic shock. Of 73 isolates tested, 31/73 (44.3%) were clindamycin resistant and 9/73 (12.9%) tested intermediate. Anaerobic-active antimicrobial therapy was received by 53/73 (72.6%). Thirty-day mortality was 11/73 (15.1%). Mortality was 30.0% (6/20) with therapy without reliable anaerobic activity and 9.4% (5/53) with anaerobic-active antimicrobial therapy (OR, 4.02; 95% CI, 0.88–19.46; $P = 0.060$). The median hospital LOS was 8.0 days. Among 30-day survivors, anaerobic active antimicrobial therapy was associated with a shorter median LOS compared to therapy without reliable anaerobic activity (8.5 vs. 12.0 days). Immunocompromised patients had higher odds of monomicrobial *C. ramosum* bacteremia than immunocompetent patients (OR 3.16, 95% CI 1.19–8.39; $p = 0.03$). Patients with polymicrobial bacteremia had higher odds of sepsis (OR, 3.89; 95% CI, 1.43–10.55; $P = 0.008$) and septic shock (OR, 5.66; 95% CI, 1.17–27.36; $P = 0.020$). Patients with malignancy or neutropenia demonstrated significantly lower odds of presenting in septic shock ($p = 0.018$; $p = 0.029$ retrospectively). Microbiological clearance was achieved in 91.3% (42/46) of evaluable cases.

Conclusions:

This largest reported cohort defines the clinical and microbiological profile of *C. ramosum* bacteremia. Frequent clindamycin nonsusceptibility is clinically actionable. Several clinical associations found on univariable analysis should be further investigated in larger studies.

Background

Clostridium ramosum is an anaerobic, gram-positive spore-forming bacterium and a component of the human intestinal microbiota [1–3]. Due to its unique cell wall structure with peptidoglycan content, *C. Ramosum* often is variably gram-positive [2–7]. In immunocompromised individuals or when the intestinal barrier is compromised, it can act as an opportunistic pathogen, leading to bacteremia, intra-abdominal infections, and soft tissue infections [2–7].

C. ramosum bacteremia is uncommon and underrepresented in the literature. *C. ramosum* accounted for 13/138 (9.4%) of *Clostridium* spp. bacteremia in a Canadian population-based study, 27/278 (9.7%) in a Japanese multicenter cohort, and 48/386 (12.4%) in a Swedish population-based cohort [8–10]. The majority of published case studies originate from Japan [2, 3, 4, 9]. However, evidence from U.S. institutions remains sparse and is largely limited to case reports and small case series. The limited recovery of anaerobic organisms in polymicrobial infections may hinder accurate diagnosis and contribute to their underrecognition [7, 11].

The primary aim of this study was to describe the clinical characteristics of patients with *C. ramosum* bacteremia. Secondary aims were to evaluate the source of bacteremia and outcomes including length of stay, antimicrobial resistance patterns, anaerobic active antimicrobial therapy, clearance of bacteremia, resistance and mortality.

Methods

This multicenter retrospective cohort study was conducted across Mayo Clinic hospitals in Jacksonville, Florida; Phoenix, Arizona; Rochester, Minnesota; and Mayo Clinic Health System site in Wisconsin. Adults (≥ 18 years) with ≥ 1 least one blood culture positive for *C. ramosum* from September 1, 2012, through December 31, 2025, were identified from microbiology records.

The index admission was the first healthcare encounter during which *C. ramosum* was recovered from blood. All charts of patients with positive blood cultures were manually reviewed to distinguish true bacteremia from contamination. Contaminant classification considered documentation by the treating or infectious diseases team, absence of clinical evidence of infection, and improvement without organism-directed therapy. After 17 contaminants were excluded, 73 patients with true bacteremia comprised the final cohort (Fig. 1).

Demographic and clinical variables included age, sex and comorbidities (inflammatory bowel disease, diabetes mellitus, hypertension, transplant history, graft-versus-host disease (GVHD) and malignancy) were abstracted from the electronic health record. Recent antineoplastic therapy (chemotherapy or

immunotherapy) was categorized based on timing relative to the index admission (≤ 2 weeks or > 2 weeks). Infection-related variables included neutropenic fever, sepsis and septic shock.

Blood culture isolates recovered from aerobic or anaerobic BACTEC bottles were identified by methods that varied over time and by laboratory at each Mayo Clinic site per its standards, including matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; Bruker Daltonics; in-house Mayo Clinic and FDA-cleared databases) and, when required, 16S rRNA gene PCR/sequencing [11]. Antimicrobial susceptibility testing was routinely performed on the first *C. ramosum* isolate recovered from blood culture per patient per episode in Rochester, Minnesota, and on clinical request at other Mayo Clinic sites. All anaerobe antimicrobial testing was performed in Rochester, MN using Etest (bioMérieux) or Clinical and Laboratory Standards Institute (CLSI) method of reference agar dilution; categorical interpretations followed the CLSI. CLSI anaerobe antimicrobial breakpoints were applied according to the published year of the CLSI M100 document [12]. Routine antimicrobial agents tested included penicillin, piperacillin-tazobactam, clindamycin, ertapenem, and metronidazole.

Both the index blood culture and concurrently collected blood culture sets were reviewed. Recovery of any additional organism from either set was classified as polymicrobial bacteremia. The presumed anatomic source of infection (for example, gastrointestinal tract, osteomyelitis, or skin and soft tissue) was distinguished from the route of bloodstream infection. An IDSA-informed clinical definition was used for catheter-related bloodstream infection (CRBSI) [13].

For assessment of microbiological clearance, all repeat blood cultures obtained after the day of the initial positive blood culture during the index hospitalization were reviewed. For assessment of microbiological clearance, all repeat blood cultures obtained after the initial positive blood culture during the index hospitalization were reviewed. Clearance was defined as negative follow-up blood cultures. When follow-up cultures were not obtained, documented clinical improvement without evidence of persistent bloodstream infection was reported separately as clinical clearance.

Antimicrobial treatment regimens were manually reviewed and documented. All patients received treatment based on sensitivity results to *C. Ramosum*. Anaerobic-active antimicrobial therapy was defined as receipt of at least one β -lactam/ β -lactamase inhibitor combination, carbapenem, or metronidazole. Therapy without reliable anaerobic activity included cephalosporin monotherapy, penicillin monotherapy, or clindamycin monotherapy, based on published susceptibility data [14, 15]. This classification was not changed by isolate-level penicillin or clindamycin susceptibility and did not assess activity against copathogens in polymicrobial bacteremia.

All statistical analyses were performed in Python 3.12. Data manipulation and descriptive statistics were conducted using the pandas and NumPy libraries, while inferential statistics and categorical comparisons were performed using the SciPy library.

Continuous variables were summarized as median (interquartile range [IQR]), and categorical variables were reported as frequencies and percentages. To evaluate associations between host factors,

microbiological presentation, and disease severity, univariable analyses were performed using Fisher's exact tests for categorical comparisons. Measures of association were reported as odds ratios (ORs) with 95% confidence intervals (CIs). A p-value of less than 0.05 was considered statistically significant. Due to the limited sample size and small number of outcome events, multivariable regression was not performed to avoid model overfitting.

Results

Baseline patient characteristics

Ninety patients with at least one blood culture positive for *C. ramosum* were identified. After manual review excluded 17 contaminants, 73 patients comprised the descriptive cohort (Fig. 1).

Baseline characteristics of patients with *C. ramosum* bacteremia are summarized in Table 1. Median age was 66.0 years (IQR, 56.0–75.0), and 44/73 (60.3%) were male. Thirty-three (45.2%) were immunocompromised, including 26 (35.6%) with active malignancy (of whom 10 had history of solid organ or hematopoietic stem cell transplant and 3 with GVHD concurrently with malignancy 21.9%), and the remaining 7 with other causes such as biologic immunosuppression (e.g., alemtuzumab for aplastic anemia) or a remote history of malignancy, currently in remission. All patients with active malignancy had recent antineoplastic therapy, of whom 16 had received antineoplastic therapy within 2 weeks before index admission. Comorbidities included hypertension 45/73 (61.6%), diabetes mellitus 23/73 (31.5%), transplant history 13/73 (17.8%), and malignancy 26/73 (35.6%).

Table 1

Baseline characteristics of the study cohort. Data are n (%) unless stated otherwise. Active malignancy was documented as active and contributing to of 73 adult patients with confirmed *C. ramosum* bacteremia identified across Mayo Clinic hospitals between September 2012 and December 2025. Continuous variables are presented as median and interquartile range (IQR), while categorical variables are presented as number and percentage.

Characteristic	n (%) or median (IQR)
Age, median (IQR), years	66.0 (56.0–75.0)
Male sex	44 (60.3)
Hypertension	45 (61.6)
Diabetes mellitus	23 (31.5)
Active malignancy contributing to immunocompromised status	26 (35.6)
Neutropenia	22 (30.1)
Neutropenic fever	16 (21.9)
Immunocompromised status	33 (45.2)
Transplant history	13 (17.8)
Graft-versus-host disease	3 (4.1)
Recent antineoplastic therapy	26 (35.6)
Antineoplastic therapy $\leq$ 2 weeks before admission	16 (21.9)

Sources of infection, clinical presentation, and microbiology

The most common infection source was gastrointestinal (32/73, 43.8%). An indwelling vascular catheter was present in 32/73 (43.8%) of patients with *C. Ramosum* bacteremia, but only 8/73 (11.0%) met the study's CRBSI definition. Other sources included osteomyelitis (8/73, 11.0%), skin and soft tissue (4/73, 5.5%), urinary (3/73, 4.1%), pulmonary (3/73, 4.1%), and dental infection (1/73, 1.4%). Sepsis occurred in 37/73 (50.7%), septic shock in 15/73 (20.5%), and neutropenic fever was documented in 16/73 (21.9%). Bacteremia was polymicrobial in 44/73 (60.3%) and monomicrobial in 29/73 (39.7%). Among 70 isolates tested for clindamycin, 31 (44.3%) were resistant, 9 (12.9%) intermediate, and 30 (42.9%) susceptible; thus, 40/70 (57.1%) were nonsusceptible.

Management and clinical outcomes

Anaerobic-active antimicrobial therapy was received by 53/73 (72.6%), and 20/73 (27.4%) received therapy without reliable anaerobic activity for *C. Ramosum* bacteremia. The median LOS was 8.0 days (IQR, 5.0–19.0). Among 30-day survivors, median LOS was 8.5 and 12.0 days for appropriate vs.

inappropriate therapy ($p = 0.85$), while among those who died within 30 days, LOS was 9.0 vs. 4.0 days, respectively ($P = 0.46$). In-hospital and 30-day all-cause mortality were each 11/73 (15.1%). Thirty-day mortality for patients receiving anaerobic active vs those without reliable anaerobic activity was 6/20 (30.0%) and 5/53 (9.4%), respectively (OR, 4.02; 95% CI, 0.88–19.46; $P = 0.060$); the CI was wide and the comparison did not show a statistically detectable association. Among 46 patients with follow-up culture results, 42/73 (91.3%) achieved microbiological or clinical clearance. For the four patients that did not clear their infection, two died (one on day 1 of hospitalization, and the other transitioned to hospice), and two had highly complex clinical courses (one with a 34-day LOS after antineoplastic treatment and the other with sigmoid colon perforation). No recurrences were observed (Table 2).

Table 2

Clinical presentation, microbiology, treatment, and outcomes of patients with *C. ramosum* bacteremia. Data are n (%) unless stated otherwise.

*Among 70 isolates tested. †Anaerobic-active antimicrobial therapy was defined as a regimen containing a β -lactam/ β -lactamase inhibitor combination, carbapenem, or metronidazole; therapy without reliable anaerobic activity included cephalosporin, penicillin, or clindamycin monotherapy. Classification was not changed by isolate-level penicillin or clindamycin susceptibility. Data derived from 73 adult patients with confirmed *C. ramosum* bacteremia treated at Mayo Clinic hospitals between September 2012 and December 2025.

Clinical presentation	n (%) or median (IQR)
Sepsis	37 (50.7)
Septic shock	15 (20.5)
Neutropenic fever	16 (21.9)
Microbiological characteristics	
Polymicrobial bacteremia	44 (60.3)
Monomicrobial bacteremia	29 (39.7)
Clindamycin resistant isolates*	31/70 (44.3)
Clindamycin intermediate isolates*	9/70 (12.9)
Clindamycin susceptible isolates*	30/70 (42.9)
Treatment and clinical outcomes	
Anaerobic-active antimicrobial therapy†	53 (72.6)
Therapy without reliable anaerobic activity†	20 (27.4)
Hospital length of stay, days	8.0 (5.0–19.0)
In-hospital mortality	11 (15.1)
30-day all-cause mortality	11 (15.1)
Microbiological or clinical clearance	42/46 (91.3)
Recurrence	0 (0)

In univariable analyses, immunocompromised patients had 3.16-fold higher observed odds of monomicrobial *C. ramosum* bacteremia than immunocompetent patients (18/33 [54.5%] vs 11/40 [27.5%]; OR, 3.16; 95% CI, 1.19–8.39; $P = 0.030$). Compared with monomicrobial *C. Ramosum* bacteremia, polymicrobial *C. Ramosum* bacteremia was associated with 3.89-fold higher observed odds of sepsis (28/44 [63.6%] vs 9/29 [31.0%]; OR, 3.89; 95% CI, 1.43–10.55; $P = 0.008$) and 5.66-fold higher observed odds of septic shock (13/44 [29.5%] vs 2/29 [6.9%]; OR, 5.66; 95% CI, 1.17–27.36; $P = 0.020$).

Lower observed odds of septic shock were estimated for patients with any history of malignancy (3/36 [8.3%] vs 12/37 [32.4%]; OR, 0.19; 95% CI, 0.05–0.74; P = 0.018) and for patients with neutropenia (1/22 [4.5%] vs 14/51 [27.5%]; OR, 0.13; 95% CI, 0.02–1.03; P = 0.029). An indwelling vascular catheter was not associated with statistically detectable odds of septic shock (4/32 [12.5%] vs 11/41 [26.8%]; OR, 0.39; 95% CI, 0.08–1.53; P = 0.150). These results were based on univariate analysis due to small number of patients (Table 3).

Table 3

Exploratory univariable comparisons. Values are n/N (%) unless stated otherwise. Fisher's exact tests were two-sided for categorical comparisons; the LOS comparison used a two-sided Mann–Whitney U test. No adjustment was made for multiple comparisons. CI, confidence interval; LOS, length of stay; OR, odds ratio.

Outcome	Comparison	Effect estimate (95% CI)	Test; P value
30-day mortality	Therapy without reliable anaerobic activity vs anaerobic-active antimicrobial therapy	30.0% (6/20) vs 9.4% (5/53); OR 4.02 (0.88–19.46)	Fisher's exact; 0.060
Median LOS (30-day survivors)	Anaerobic-active antimicrobial therapy vs therapy without reliable anaerobic activity	8.5 vs 12.0 days	Mann–Whitney U; 0.850
Monomicrobial bacteremia	Immunocompromised vs immunocompetent	54.5% (18/33) vs 27.5% (11/40); OR 3.16 (1.19–8.39)	Fisher's exact; 0.030
Sepsis	Polymicrobial vs monomicrobial bacteremia	63.6% (28/44) vs 31.0% (9/29); OR 3.89 (1.43–10.55)	Fisher's exact; 0.008
Septic shock	Polymicrobial vs monomicrobial bacteremia	29.5% (13/44) vs 6.9% (2/29); OR 5.66 (1.17–27.36)	Fisher's exact; 0.020
Septic shock	Any malignancy history vs none	8.3% (3/36) vs 32.4% (12/37); OR 0.19 (0.05–0.74)	Fisher's exact; 0.018
Septic shock	Neutropenia vs none	4.5% (1/22) vs 27.5% (14/51); OR 0.13 (0.02–1.03)	Fisher's exact; 0.029

Discussion

This multicenter largest-to-date descriptive cohort characterizes the clinical phenotype, microbiology, management, and outcomes of 73 adults with *C. ramosum* bacteremia (Table 4). Polymicrobial bacteremia occurred predominantly in immunocompetent hosts and was associated with an increased risk of sepsis and septic shock. Monomicrobial bacteremia was more frequently observed among immunocompromised patients. Underlying malignancy and neutropenia were not associated with an increased risk of sepsis or septic shock. This finding may reflect heightened clinical vigilance, closer

follow-up, and more frequent use of empiric antimicrobial therapy in these high-risk populations, facilitating earlier recognition of febrile illness, prompt medical evaluation, and timely initiation of appropriate antimicrobial treatment. Receipt of anaerobic-targeted antimicrobial therapy in patients with *C. Ramosum* monomicrobial and polymicrobial bacteremia were associated with a shorter length of hospital stay and a trend toward lower 30-day mortality. These outcome results were based on univariable analysis of small cohort and should be evaluated in future on larger cohort.

Table 4

Published cohorts containing *C. ramosum* bacteremia. NR, mortality not reported. Mortality is shown only when reported for the *C. ramosum* subset.

Study	Country	Study period	<i>C. ramosum</i> cases, n	Mortality, n/N (%)
Sarasoja et al. [10]	Sweden	2014–2019	48	NR
Okazaki et al. [9]	Japan	2007–2021	27	NR
Leal et al. [8]	Canada	2000–2006	13	NR
Shinzato et al. [2]	Japan	2009–2020	7	4/7 (57.1)
Gollapudi et al. [25]	United States	2013–2017	5	3/5 (60.0)
Present study	United States	2012–2025	73	11/73 (15.1)

C. ramosum is a gastrointestinal commensal that may enter the bloodstream after mucosal disruption and translocation into the bloodstream, particularly in older adults and patients with malignancy, neutropenia, diabetes mellitus, liver cirrhosis, heavy alcohol use, or underlying gastrointestinal disease [2, 7, 9, 16]. Consistent with the Swedish cohort [10], our cohort was comprised predominantly of male patients in their mid-60s, and had a substantial burden of comorbidities, including obesity, hypertension, diabetes mellitus, malignancy and solid organ transplantation.

The gastrointestinal tract was the most common source of *C. ramosum* bacteremia, followed by central line–associated bloodstream infections and osteomyelitis, and less frequently, skin and soft tissue infections (including diabetic foot ulcers and pressure injuries). Less common sources include urinary tract, pulmonary, and dental infections. Rare reports from the literature describe arterial thrombosis with mesenteric ischemia, SARS-CoV-2–associated immunosuppression, and severe sepsis complicated by hemolytic anemia as associated with *C. ramosum* bacteremia [2, 7, 16–19].

Given that *C. ramosum* colonizes up to 83% of the adult intestines, it is not surprising that the gastrointestinal tract is the predominant source of bacteremia. Clostridial bacteremia is also associated with substantial morbidity and mortality in patients with malignancy [1, 20]. In our cohort, 48.6% of patients had an underlying malignancy and 35.1% had recently received cytotoxic therapy, comparable to the Swedish cohort, in which 42% of patients with *C. ramosum* bacteremia had malignancy and 27% were immunocompromised [10]. Both malignancy and anticancer therapy impair host defenses, while gastrointestinal, genitourinary, and hematologic malignancies further predispose patients to *Clostridium*

spp. bacteremia through mucosal disruption, tissue hypoxia and necrosis [21]. Although *C. ramosum* is generally considered a low-virulence organism, IgA protease production may facilitate intestinal mucosal invasion and bloodstream translocation in immunocompromised hosts, a process that may be exacerbated by glucocorticoid-induced impairment of intestinal barrier integrity during chemotherapy [1, 22]. In our cohort, 30% of patients were neutropenic on admission and 16/73 (21.9%) had neutropenic fever. Recovery of neutrophil counts during infection has been associated with higher cure rates (64% vs. 37%; $P = 0.01$), whereas persistent severe neutropenia (< 100 cells/ μ L) is associated with poor outcomes [21]. Although our results indicate that malignancy and neutropenia were associated with the lower observed odds of septic shock, this association could be a result of high vigilance of neutropenic patients and early initiation of broad spectrum antibiotic treatment in neutropenic patients with fever in general.

Antimicrobial susceptibility findings are among the most clinically actionable observations. Clindamycin resistance was present in 31/70 (44.3%) isolates and a further 9/70 (12.9%) were intermediate. The resistance proportion exceeded 5% and 16% reported in two earlier in vitro series [2, 15, 23]. These data argue against relying on clindamycin as empirical monotherapy for suspected *C. ramosum* bacteremia [2, 7, 9]. Treatment of *C. ramosum* bacteremia primarily includes β -lactams, carbapenems, and metronidazole, due to low MICs reported in prior studies [2, 3, 7, 14]. Prior studies have reported variable susceptibility to penicillin, clindamycin, and cephalosporins, likely related to β -lactamase production. Reduced susceptibility to tetracycline and moxifloxacin has been reported, although multidrug resistance remains uncommon. Fluoroquinolones other than moxifloxacin generally have limited anaerobic activity [3, 7, 14, 23]. Source control remains an essential adjunct for infections requiring drainage or debridement [2, 7]. Prior studies suggested that effective management of *C. ramosum* bacteremia requires agents with reliable anaerobic activity, especially in immunocompromised patients, where delayed appropriate therapy may contribute to adverse outcomes [2, 7, 13, 14]. In this study, the therapy categories reflected expected *C. ramosum* activity, even though all patients received therapy based on *C. ramosum* blood culture sensitivities and included appropriate activity against copathogens based on sensitivity results.

In our cohort, only 72.6% of patients received anaerobic targeted therapy, leaving over one-quarter treated with regimens lacking adequate anaerobic activity. Observed 30-day mortality was higher among patients who received antimicrobial therapy without reliable anaerobic activity than among those who received anaerobic-active therapy (30.0% vs 9.4%; OR, 4.02; 95% CI, 0.88–19.46; $P = .060$), representing a strong trend toward worse outcomes, although statistical significance was not reached, likely due to limited sample size.

Polymicrobial bacteremia occurred in 44/73 (60.3%) cases, consistent with prior clostridial bacteremia cohorts [2, 7, 9, 10]. Polymicrobial disease is often associated with underlying gastrointestinal pathology, including perforation, ischemia, and abscess formation, whereas monomicrobial infection has been reported in soft tissue infections, Fournier's gangrene, and infections in immunocompromised hosts [4,

16, 19]. In polymicrobial specimens, faster-growing organisms may predominate, potentially obscuring the clinical significance of *C. ramosum* and leading to under-recognition or misattribution [2, 24].

Among *Clostridium* spp., *C. ramosum* is reported as one of the species associated with the highest case-fatality rates [8]. Despite appropriate therapy, mortality remains substantial, with a Japanese case series reporting 57% mortality (4/7 patients) [2], and a larger multicenter cohort demonstrating 25.9% in-hospital mortality, with approximately one-third of deaths occurring within three days of the first positive blood culture [9]. In a small U.S. series of immunocompromised patients, mortality reached 60% (3/5), all of whom had hematologic malignancies [25]. Independent predictors of in-hospital mortality include hepato-pancreato-biliary malignancy, chronic heart failure, acute renal failure, elevated Pitt bacteremia score and pneumonia as the infection source [9]. Across large population-based studies in Sweden, Canada and Israel, reported mortality for clostridial bacteremia ranges from 26% to 33% [8, 26,10]. These findings highlight the importance of early identification, prompt initiation of appropriate antimicrobial therapy, and aggressive source control. In our cohort, 30-day and in-hospital mortality were each 15.1%, lower than previously reported series, with higher mortality observed among patients receiving inappropriate antimicrobial therapy.

The median hospital LOS in our cohort was 8 days, comparable to prior reports of clostridial bacteremia of 10 days [10]. Among 30-day survivors, inappropriate antimicrobial therapy was associated with longer hospitalization (12 vs. 8.5 days). In contrast, patients who died within 30 days and received inappropriate therapy had shorter hospital stays (4 vs. 9 days), likely reflecting more fulminant disease and early death rather than faster recovery.

Strengths and limitations

This study represents the largest reported cohort of *C. ramosum* bacteremia to date and provides a descriptive benchmark for future work. A key strength of the study is the large and geographically diverse patient population drawn from both rural and academic centers across four U.S. states, reflecting broad variation in patient demographics and clinical settings. Additional strengths include the inclusion of a substantial number of solid organ and hematopoietic stem cell transplant recipients.

This study has several limitations. Its retrospective design limits control over data completeness and the timing of clinical variables. In addition, the rarity of *C. ramosum* bacteremia resulted in a small cohort, limiting statistical power and precluding robust multivariable analyses. Due to the limited number of events and risk of model overfitting, multivariable regression was not performed

Conclusions

This multicenter retrospective cohort defines the clinical and microbiological profile of *C. ramosum* bacteremia. Gastrointestinal sources and polymicrobial bacteremia were common, and sepsis occurred in one-half of patients. The infection frequently presented in a polymicrobial context which was associated with increased disease severity, including sepsis and septic shock, whereas monomicrobial

infection was more common among immunocompromised hosts. Malignancy and neutropenia were associated with lower odds of septic shock, suggesting potential heightened clinical vigilance, closer follow-up, and more frequent use of empiric antimicrobial therapy in these high-risk populations. Marked increase in clindamycin resistance from previous reports is clinically actionable. Receipt of appropriate anaerobic coverage was associated with improved 30-day outcomes, potentially indicating need for anaerobic active therapy beyond relying only on sensitivity data. Overall, these findings emphasize the need for heightened clinical awareness, accurate microbiological identification, and optimized antimicrobial and source-control strategies to improve outcomes in this high-risk population.

Abbreviations

CI	confidence interval
CLSI	Clinical and Laboratory Standards Institute
CRBSI	catheter-related bloodstream infection
GVHD	graft-versus-host disease
IQR	interquartile range
LOS	length of stay
MALDI-TOF MS	matrix-assisted laser desorption/ionization time-of-flight mass spectrometry
OR	odds ratio.

Declarations

Ethics approval and consent to participate: The Mayo Clinic Institutional Review Board approved the study (protocol 22-005697) and waived informed consent because of the retrospective design. The study was conducted in accordance with the Declaration of Helsinki and applicable requirements for confidentiality and data protection.

Consent for publication: Not applicable.

Availability of data and materials:

All data generated and analyzed during this study are included in this article and its supplementary information files.

Competing interests: The authors declare that they have no competing financial or personal conflicts of interest.

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Authors' contributions:

Tatjana Gavranic: Conceptualization, Methodology, Investigation, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing, Project Administration.

Kassandra Stoddard: Data Curation, Investigation, Writing – Review & Editing.

Muhammad W. Tahir: Formal Analysis, Methodology, Data Interpretation, Writing – Review and Editing.

Marko Gorasevic: Investigation, Literature Review, Writing – Review & Editing.

Melissa Cortes: Data Curation, Investigation, Writing – Review & Editing.

Libardo Rueda Prada: Investigation, Writing – Review & Editing.

Aleksandra Murawska Baptista: Investigation, Writing – Review & Editing.

Ricardo J. Pagan: Supervision, Methodology, Writing – Review & Editing.

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Audrey N. Schuetz: Methodology, Validation, Microbiological Investigation, Supervision, Writing – Review & Editing.

Igor Dunic: Conceptualization, Methodology, Supervision, Writing – Review & Editing.

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Figures

Patients with ≥ 1 positive
C. ramosum blood culture
(n = 90)



Excluded: blood culture contaminants after manual chart review
(n = 17)



Final study cohort with true *C. ramosum* bacteremia
(n = 73)

Figure 1

Patient selection flow diagram. Ninety adults with at least one positive *C. ramosum* blood culture were identified from September 2012 through December 2025. Manual chart review excluded 17 contaminants, leaving 73 patients with true *C. ramosum* bacteremia.